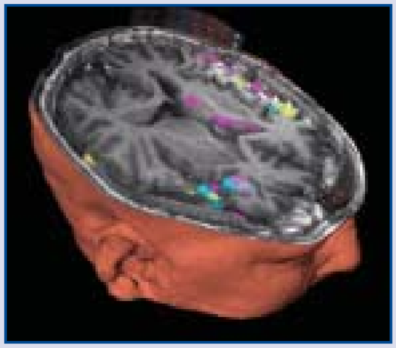
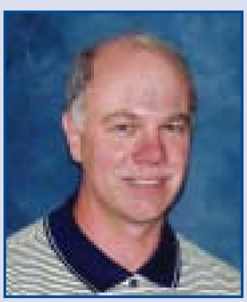
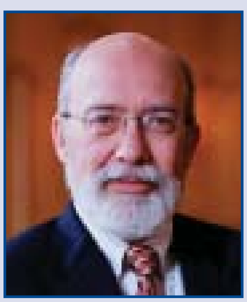


Integrated Imaging: Improving Epilepsy Surgery

NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING

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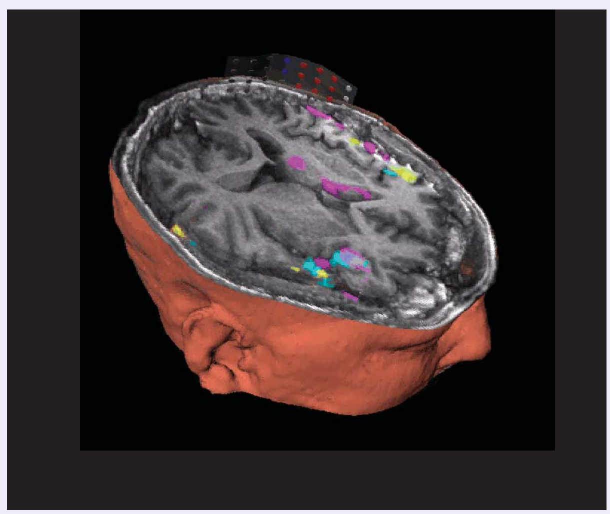
Integrated Imaging: Improving Epilepsy Surgery

For those with epilepsy, seizures can disrupt daily routines, from going to school to holding a job to driving a car. Medication offers relief for most patients, but for the small percentage whose seizures are debilitating and untreatable, surgical removal of damaged brain tissue may be the best option. A new imaging system now being developed by an interdisciplinary team of researchers may shorten surgery times and greatly improve the success rate of this sometimes-risky procedure by allowing surgeons to more precisely pinpoint, and then remove, seizure-causing brain regions.

The new system integrates detailed information about brain anatomy, biochemistry, and electrical changes that occur during seizures, explains Dr. James Duncan, professor of diagnostic radiology, biomedical engineering, and electrical engineering at Yale University. As principal investigator of a five-year, $7.1 million research project funded since 2002 by the National Institute of Biomedical Imaging and Bioengineering (NIBIB), Dr. Duncan heads a multi-institutional team of engineers, scientists, and physicians located at Yale, Albert Einstein College of Medicine, the University of Minnesota, and BrainLAB, Inc., a German company that specializes in image-guided surgery. Dr. Duncan presented early results of this ongoing research project at a January 2004 meeting of the NIBIB Advisory Council.



Researchers are developing an imaging system that may lead to better surgical treatments for epilepsy patients. This image shows normal brain activity.

Typically, removal of seizure-causing brain tissue requires patients to undergo two seven-hour surgeries. During the first surgery, electrodes are placed on or inserted into brain areas suspected of causing seizures, usually detectable as sudden and intense bursts of electrical energy. Information gleaned from electrode monitoring allows surgeons to map the source of the seizure activity. During the second procedure, performed a few weeks later, surgeons follow the map to the damaged brain tissue, which is carefully removed.

With the new imaging system, the first surgery might eventually be omitted, since high-resolution images of the brain's anatomy, biochemistry, and electrical activity would be integrated before and during the operation. This detailed information would help surgeons to plan and perform the procedure with greater precision.

Neurosurgeon Dr. Dennis Spencer reports that the new prototype system provides a much more precise placement of electrodes and accurate anatomical correlation with chemical abnormalities and function. Dr. Spencer, acting dean of the Yale School of Medicine and a co-investigator on the NIBIB grant, has used the prototype imaging system on more than 50 patients, about half of whom are children. "The earlier you can correct their symptoms, the better," he notes.

With the new imaging system, surgeons can correlate a wide variety of preoperative brain images, including biochemical information obtained via magnetic resonance spectroscopy (MRS) and computerized assessments of electrical activity obtained via electrode monitoring. Magnetic resonance images (MRI) taken prior to surgery are also available by way of pull-down screens in the operating room, along with projected displays of microscope-based images during the surgery. The MRI provides anatomical details and reveals important functional areas of the brain, like language regions, that must not be damaged during the operation. The researchers are also beginning to acquire and integrate images that represent blood flow in the brain. "By coregistering blood flow, electrical activity, and biochemical activity, we can more precisely see where brain activity is abnormal," says Dr. Spencer.

Brain anatomy is also monitored during the surgery, since brain tissue tends to decompress by as much as 1 centimeter when exposed during the operation. Even a small shift of brain tissues can throw off the surgeons' calculations for locating seizure-causing areas. To avert such problems, Dr. Spencer and his colleagues have set up stereotactic cameras in the operating room that track the movement of the exposed brain surface from slightly different angles, thereby adding a perception of depth. Images from the cameras are then coupled with a computerized model, developed by Dr. Duncan and his colleagues, that predicts how the entire brain volume is shifting. This rapid modeling may allow surgeons to account for brain tissue deformation.

"Using imaging and stereotactic cameras in the operating room is much less expensive than installing a $3-million MRI system in the operating room," as is done for some other image-guided surgery efforts, says Dr. Spencer. In contrast, he says, the cost for the modeling system developed by the Yale team and their colleagues is about $100,000.

Over the next several years, Dr. Spencer expects the research team will develop a neurostimulator that could be implanted in the brain to short-circuit seizures and thus reduce symptoms. The neurostimulator would be programmed to shock the brain when a seizure-associated electrical pattern occurs. The pattern location would be determined by the prototype imaging system now under development, Dr. Spencer explains.
The team's 10- to 15-year-goal is to develop a procedure in which surgeons insert a

biosensor along with a drug-delivery system into the brains of epilepsy patients. The system would trigger release of a drug that blocks seizures before they begin.

By taking a look at the entire brain—its chemistry, anatomy, and electrical activity—surgeons are better able to tackle epilepsy at its source. "This multidimensional approach is leading to a better understanding of the biochemical, functional, and anatomical changes in the brain that epilepsy creates," Dr. Duncan notes.

Patient Profiles

Forty-seven-year-old ***Juliet Henry***, a former law office supervisor and grandmother of 12, tells how when she was a teenager her epilepsy had been misdiagnosed as emotional imbalance. "For years they said I was crazy and had me going to psychiatrists," says Juliet. Even after she was properly diagnosed in her early 20s, there were long stretches of time when she would have 15 to 25 epileptic seizures a day. As a result, she lost her job, her driver's license, and a good portion of her life to the disease.

Twenty-year-old college student ***Sarah Perruccio*** fared little better. Diagnosed with epilepsy at age 12, she remembers how the medication she was taking for her epilepsy would give her toxic reactions, and how epilepsy affected her short-term memory. She also remembers asking her teachers not to call on her in class because even the relatively mild seizures affected her speech.

Both Juliet and Sarah have separate—yet similarly challenging and heroic—stories to tell about their battles with epilepsy. Both struggled with the disease for years (in Juliet's case, decades). Both tried medications that at best diminished or halted their seizures for limited periods of time only. Both underwent brain surgery, performed by Yale neurosurgeon Dr. Dennis Spencer, to treat their epilepsy. And both are now, very gratefully, seizure free.

What Sarah did not know at the time of her surgery, in June 2002, was that she would be among the first to benefit from new prototype imaging technologies, now being more fully developed by Dr. Spencer, Dr. James Duncan, and their colleagues, with funding from NIBIB. With further development and testing, the new technologies may dramatically enhance the surgical treatment of epilepsy and other neurological disorders.

About Epilepsy

Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked, and often disabling seizures that arise from uncontrollable activation of particular brain regions. The disease affects approximately one percent of the U.S. population—individuals of all ages, races, and socioeconomic backgrounds.

Many people with epilepsy live in constant fear of having seizures, especially in public. What makes seizures so dangerous is that they can cause accidental injury, cognitive decline, sudden death, and psychological impairment.

"I didn't have many friends in high school," says Sarah. "I wouldn't hang out with kids who wouldn't know what to do if I had a seizure." In Juliet's case, there was a five-year period when her seizures were so bad that she could not be left alone for any length of time, and she relied heavily on her family and children for assistance.

The Promise of New Technologies

Individuals with epilepsy are initially treated with medications, which are usually sufficient to control their seizures. But some patients have a more intractable form of the disease that can be treated only by surgical removal of the seizure-causing brain tissue.

Brain surgery for epilepsy often requires two separate operations: the first includes the use of electrodes to help surgeons map the brain regions suspected of causing seizures. In the second surgery, which usually takes place a week or more after the first, the surgeon follows the map created in the first surgery to carefully remove damaged brain tissue. Eventually, with the new integrated imaging technologies now under development, Drs. Spencer and Duncan hope to eliminate the need for the first exploratory surgery and to provide more accurate data when intracranial electrodes are necessary.

One of the exciting aspects of this particular research is the coregistration system being developed. The system, which maps blood flow, electrical activity, and biochemical activity, provides a more accurate picture of the location of abnormal chemicals. “This will improve patient comfort and reduce the time it takes to operate,” says Dr. Spencer.

Juliet underwent her brain surgery prior to the complete development of the new imaging system. In her case, during the first surgery, Dr. Spencer mapped the placement of electrodes on her brain using an older computer program that requires hand tracing the electrodes on a postoperative MRI scan. During the second surgery to remove damaged brain tissue, the “map” was taped to the wall of the operating room for Dr. Spencer to follow. Fortunately for Juliet, even without use of the new imaging technology, her surgery was a complete success and today she is seizure free.

In Sarah’s case, Dr. Spencer had access to some of the early technological developments that have since become part of the new imaging system. The pilot data provided more accurate localization of the intracranial electrodes used in Sarah’s surgery.

On the Horizon

In addition to advances in imaging technology, researchers supported by NIBIB are also working on new therapies that could greatly improve the lives of those with epilepsy. Within the next five years, for example, researchers hope to perfect a stimulation therapy whereby electrodes are placed on the brain to record electrical events. By using a computer to analyze waveforms, clinicians will be able to detect seizures before patients exhibit symptoms. An implanted defibrillator the size of a Zippo cigarette lighter would be used to stimulate the brain and short-circuit seizures.

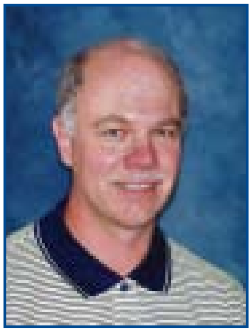
In the next five to 10 years, it is possible that a therapy based on imaging and coregistration of biochemical abnormalities could restore normal chemical function to people with epilepsy by infusing a chemical that would dampen the electrical system before seizure activity even starts.

In the meantime, Sarah and Juliet are just happy to be seizure free.

Sarah, interviewed by cell phone for this profile while she rode a train from Venice to Florence, says that life is all about second chances. “I was given mine and now I just want to give something back.” Now majoring in social work at Gordon College in Massachusetts, Sarah has been studying in Italy while on a semester abroad program. She says she never dreamed she’d be able to travel abroad and meet so many new people. “Before my surgery, I didn’t even have time or the energy to put into relationships with other people,” she says. Although some of that feeling still lingers, she adds, “I’m gaining confidence in myself all the time.”

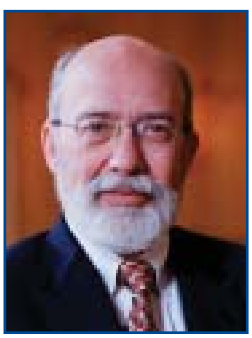
For her part, Juliet is seriously considering reentering the workforce, perhaps in her former role as a law office supervisor. For now, she spends her time providing childcare for her grandchildren and sewing. “Where once my family cared for me, now I’m able to care for them,” she says with great delight. “I feel blessed to be able to hold my grandbabies without the fear of seizures.”

Doctor Biographies



James S. Duncan, Ph.D.

James S. Duncan, Ph.D., is professor of diagnostic radiology and electrical engineering, and director of the biomedical engineering program at Yale University. Much of Dr. Duncan's research focuses on enabling computers to recognize objects in biomedical images, particularly objects that change their shape, such as the heart. Dr. Duncan is also leading the development of an integrated imaging system to help neurosurgeons more precisely pinpoint, and then remove, damaged brain tissue from patients with epilepsy. Dr. Duncan received a Ph.D. in electrical engineering from the University of Southern California and has been elected as a Fellow of both the American Institute for Medical and Biological Engineering and the Institute of Electrical and Electronics Engineers.



Dennis D. Spencer, M.D.

Dennis D. Spencer, M.D., is the Harvey and Kate Cushing Professor of Neurosurgery and interim dean of the Yale School of Medicine. He directs the surgical arm of the Yale Epilepsy Program, one of the world's principal epilepsy centers. Dr. Spencer developed a widely used surgical approach for patients with temporal lobe epilepsy and helped to design the first computerized brain-imaging system for use in neurosurgery. He is now overseeing a research project on metabolic and energy deficiencies in epileptogenic brain tissue and is developing a new epilepsy treatment that involves implanting computerized electrodes into the brain to short-circuit incipient seizures. A graduate of Washington University School of Medicine, Dr. Spencer did his neurosurgical residency at Yale.

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